US Army Medical Research and Materiel

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Live Attenuated Virus Vaccines for Western Equine Encephalitis Virus, Eastern Equine Encephalitis Virus, and Venezuelan Equine Encephalitis Virus IE and IIIA Variants

Features and advantages:

- **WEE and VEE IE cDNAs and VEE IIIA and EEE chimeric viruses protected vaccinated mice against challenge**
- **Provides greater safety margin because viruses are attenuated**
- **Could be inactivated to allow production to occur under lower biocontainment levels**
- **Would require significantly less material to produce the new vaccines than current vaccines**

Patent Status

Patent No.: 6,261,570 **Available from:** www.uspto.gov **Issued:** July 17, 2001 **Docket No.:** RID 96-01

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KEYWORDS: WEE, VEE, EEE, attenuated alphaviruses, vaccine

This invention provides live attenuated vaccines against western and eastern equine encephalitis (WEE and EEE respectively) and Venezuelan equine encephalitis (VEE) subtype IE and IIIA viruses. The invention includes cDNAs coding for infectious WEE and VEE IE, cDNAs coding for the structural proteins of VEE IIIA, novel attenuating mutations of WEE and VEE IE, and attenuated chimeric alphaviruses.

The WEE, EEE, and VEE viruses are members of a large group of mosquito-borne RNA viruses that are found throughout much of the world. The current WEE, EEE, and VEE IA/B vaccines are formalin-inactivated preparations and are poorly immunogenic, requiring multiple inoculations with frequent boosters. The invention provides vaccines comprised of full-length cDNA copies of the genomes of WEE or VEE IE which have been altered such that the RNA produced from the cDNA, and the virus produced therefrom, is attenuated. The VEE IIIA and EEE vaccines are novel chimeric viruses which include the newly discovered structural protein gene of VEE IIIA. The VEE IIIA vaccine is a clone in which the nonstructural protein gene sequences were from VEE IA/B and the structural protein gene sequences were from VEE IIIA. The EEE chimeric virus consists of structural protein genes of EEE inserted into the infectious clone in place of the WEE structural protein genes. The clones protect vaccinated mice against challenge with virulent, wild-type Mucambo virus (VEE IIIA) and EEE virus, respectively.

Depending on the non-WEE sequences substituted for the WEE structural genes, the invention could be used to express antigens from other alphaviruses, such as Chikungunya and Semliki Forest, or from foreign antigens in order to vaccinate

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